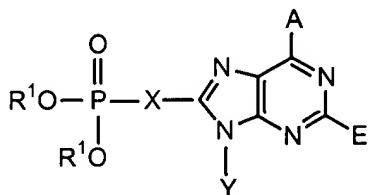
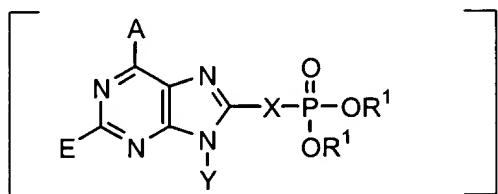


IN THE CLAIMS

Claims 2-33, 40 and 43 were cancelled without prejudice.

Claims 1, 34-37, 39, and 42 were amended as follows with the noted changes:

1. (Amended) A compound of formula 1:



wherein

A is selected from the group consisting of -NR⁸₂, -NHSO₂R³, -OR⁵, -SR⁵, [halogen] halo, lower alkyl, -CON(R⁴)₂, [guanidine, amidine,] guanidino, amidino, -H, and perhaloalkyl;

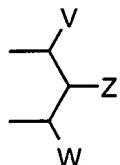
E is selected from the group consisting of -H, [halogen] halo, lower alkylthio, lower perhaloalkyl, lower alkyl, lower alkenyl, lower alkynyl, lower alkoxy, -CN, and -NR⁷₂;

X [is selected from the group consisting of alkylamino, alkyl, alkenyl, alkynyl, alkyl(carboxyl), alkyl(hydroxy), alkyl(phosphonate), alkyl(sulfonate), aryl, alkylaminoalkyl, alkoxyalkyl, alkylthioalkyl, alkylthio, alicyclic, 1,1-dihaloalkyl, carbonylalkyl, aminocarbonylamino, alkylaminocarbonyl, alkylcarbonylamino, aralkyl, and alkylaryl, all optionally substituted; or] together with Y forms a cyclic group [including] selected from the group of cyclic alkyl, heterocyclic, and aryl;

[Y is selected from the group consisting of -H, alkyl, alkenyl, alkynyl, aryl, alicyclic, aralkyl, aryloxyalkyl, alkoxyalkyl, -C(O)R³, -S(O)₂R³, -C(O)-OR³, -CONHR³, -NR²₂, and -OR³, all except H are optionally substituted; or together with X forms a cyclic group including aryl, cyclic alkyl, and heterocyclic;]

R¹ is independently selected from the group consisting of -H, alkyl, aryl, [alicyclic] heteroalicyclic where the cyclic moiety contains a carbonate or thiocarbonate, -C(R²)₂-aryl,

[alkylaryl] -alk-aryl, $-C(R^2)_2OC(O)NR^2_2$, $-NR^2-C(O)-R^3$, $-C(R^2)_2-OC(O)R^3$, $-C(R^2)_2-O-C(O)OR^3$, $-C(R^2)_2OC(O)SR^3$, [alkyl-S-C(O)R³] -alk-S-C(O)R³, [alkyl-S-S-alkylhydroxy] -alk-S-S-alkylhydroxy, and [alkyl-S-S-S-alkylhydroxy] -alk-S-S-S-alkylhydroxy, or together R¹ and R¹ are [-alkyl-S-S-alkyl-] -alk-S-S-alk- to form a cyclic group, wherein each "alk" is an independently selected alkylene, or together R¹ and R¹ are



wherein

V and W are independently selected from the group consisting of hydrogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, 1-alkynyl, and -R⁹; or

together V and Z are connected via a chain of 3-5 atoms, [optionally 1 heteroatom] only one of which can be a heteroatom, to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxy carboxy, or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus; or

together V and W are connected via a chain of [to form a cyclic group containing] 3 carbon atoms to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxy carboxy, alkylthiocarboxy, hydroxymethyl, [and] or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus;

Z is selected from the group consisting of -CH₂OH, -CH₂OCOR³, -CH₂OC(O)SR³, -CH₂OCO₂R³, -SR³, -S(O)R³, -CH₂N₃, -CH₂NR²₂, -CH₂Ar, -CH(Ar)OH, -CH(CH=CR²R²)OH, -CH(C≡CR²)OH, and -R²;

with the provisos that:

- a) V, Z, W are not all -H; and
- b) when Z is -R², then at least one of V and W is not -H or -R⁹;

R² is selected from the group consisting of R³ and -H;

R³ is selected from the group consisting of alkyl, aryl, alicyclic, heteroalicyclic, and aralkyl;

R⁴ is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, and lower aryl;

R^5 is selected from the group consisting of lower alkyl, lower aryl, lower aralkyl, lower heteroalicyclic, and lower alicyclic;

R^6 is independently selected from the group consisting of -H, and lower alkyl;

R^7 is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, lower aryl, and $-C(O)R^{10}$;

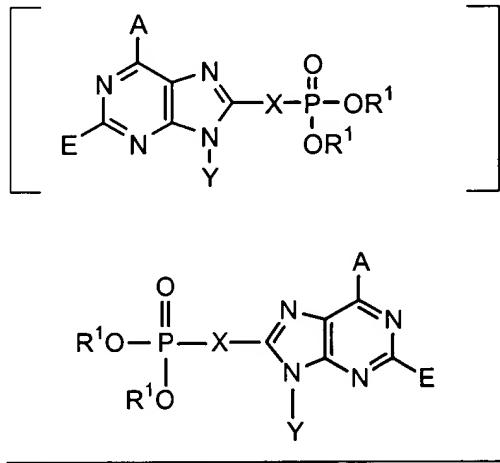
R^8 is independently selected from the group consisting of -H, lower alkyl, lower aralkyl, lower aryl, lower alicyclic, $-C(O)R^{10}$, or together [they] said R^8 groups form a bidendate [alkyl] alkylene;

R^9 is selected from the group consisting of alkyl, aralkyl, heteroalicyclic, and alicyclic;

R^{10} is selected from the group consisting of -H, lower alkyl, $-NH_2$, lower aryl, and lower perhaloalkyl;

R^{11} is selected from the group consisting of alkyl, aryl, $-OH$, $-NH_2$ and $-OR^3$; and pharmaceutically acceptable prodrugs and salts thereof.

34. (Amended) A method of treating an animal for diabetes mellitus, comprising administering to said animal a therapeutically effective amount of a compound of formula (1):



wherein

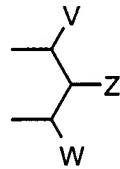
A is selected from the group consisting of $-NR^8_2$, $-NHSO_2R^3$, $-OR^5$, $-SR^5$, [halogen] halo, lower alkyl, $-CON(R^4)_2$, [guanidine, amidine,] guanidino, amidino, -H, and perhaloalkyl;

E is selected from the group consisting of -H, [halogen] halo, lower alkylthio, lower perhaloalkyl, lower alkyl, lower alkenyl, lower alkynyl, lower alkoxy, -CN, and $-NR^7_2$;

X [is selected from the group consisting of alkylamino, alkyl, alkenyl, alkynyl, alkyl(carboxyl), alkyl(hydroxy), alkyl(phosphonate), alkyl(sulfonate), aryl, alkylaminoalkyl, alkoxyalkyl, alkylthioalkyl, alkylthio, alicyclic, 1,1-dihaloalkyl, carbonylalkyl, aminocarbonylamino, alkylaminocarbonyl, alkylcarbonylamino, aralkyl, and alkylaryl, all optionally substituted; or] together with Y forms a cyclic group [including] selected from the group of cyclic alkyl, heterocyclic, and aryl;

[Y is selected from the group consisting of -H, alkyl, alkenyl, alkynyl, aryl, alicyclic, aralkyl, aryloxyalkyl, alkoxyalkyl, $-C(O)R^3$, $-S(O)_2R^3$, $-C(O)-OR^3$, $-CONHR^3$, $-NR^2_2$, and $-OR^3$, all except H are optionally substituted; or together with X forms a cyclic group including aryl, cyclic alkyl, and heterocyclic;]

R^1 is independently selected from the group consisting of -H, alkyl, aryl, [alicyclic] heteroalicyclic where the cyclic moiety contains a carbonate or thiocarbonate, $-C(R^2)_2$ -aryl, [alkylaryl] -alk-aryl, $-C(R^2)_2OC(O)NR^2_2$, $-NR^2-C(O)-R^3$, $-C(R^2)_2-OC(O)R^3$, $-C(R^2)_2-O-C(O)OR^3$, $-C(R^2)_2OC(O)SR^3$, [alkyl-S-C(O)R³] -alk-S-C(O)R³, [alkyl-S-S-alkylhydroxy] -alk-S-S-alkylhydroxy, and [alkyl-S-S-alkylhydroxy] -alk-S-S-alkylhydroxy, or together R^1 and R^1 are [-alkyl-S-S-alkyl-] -alk-S-S-alk- to form a cyclic group, wherein each "alk" is an independently selected alkylene, or together R^1 and R^1 are



wherein

V and W are independently selected from the group consisting of hydrogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, 1-alkynyl, and $-R^9$; or

together V and Z are connected via a chain of 3-5 atoms, [optionally 1 heteroatom] only one of which can be a heteroatom, to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxy carboxy, or aryloxy carboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus; or

together V and W are connected via a chain of [to form a cyclic group containing] 3 carbon atoms to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxy carboxy,

alkylthiocarboxy, hydroxymethyl, [and] or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus;

Z is selected from the group consisting of -CH₂OH, -CH₂OCOR³, -CH₂OC(O)SR³, -CH₂OCO₂R³, -SR³, -S(O)R³, -CH₂N₃, -CH₂NR²₂, -CH₂Ar, -CH(Ar)OH, -CH(CH=CR²R²)OH, -CH(C≡CR²)OH, and -R²;

with the provisos that:

- a) V, Z, W are not all -H; and
- b) when Z is -R², then at least one of V and W is not -H or -R⁹;

R² is selected from the group consisting of R³ and -H;

R³ is selected from the group consisting of alkyl, aryl, alicyclic, heteroalicyclic, and aralkyl;

R⁴ is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, and lower aryl;

R⁵ is selected from the group consisting of lower alkyl, lower aryl, lower aralkyl, lower heteroalicyclic, and lower alicyclic;

R⁶ is independently selected from the group consisting of -H, and lower alkyl;

R⁷ is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, lower aryl, and -C(O)R¹⁰;

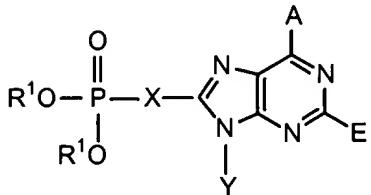
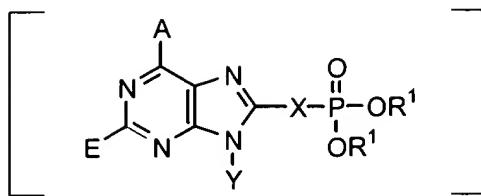
R⁸ is independently selected from the group consisting of -H, lower alkyl, lower aralkyl, lower aryl, lower alicyclic, -C(O)R¹⁰, or together [they] said R⁸ groups form a bidendate [alkyl] alkylene;

R⁹ is selected from the group consisting of alkyl, aralkyl, heteroalicyclic, and alicyclic;

R¹⁰ is selected from the group consisting of -H, lower alkyl, -NH₂, lower aryl, and lower perhaloalkyl;

R¹¹ is selected from the group consisting of alkyl, aryl, -OH, -NH₂ and -OR³; and pharmaceutically acceptable prodrugs and salts thereof.

35. (Amended) A method of lowering blood glucose levels in an animal in need thereof, comprising administering to said animal a pharmaceutically acceptable amount of a compound of formula (1):



wherein

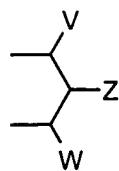
A is selected from the group consisting of -NR⁸, -NHSO₂R³, -OR⁵, -SR⁵, [halogen] halo, lower alkyl, -CON(R⁴)₂, [guanidine, amidine,] guanidino, amidino, -H, and perhaloalkyl;

E is selected from the group consisting of -H, [halogen] halo, lower alkylthio, lower perhaloalkyl, lower alkyl, lower alkenyl, lower alkynyl, lower alkoxy, -CN, and -NR⁷₂;

X [is selected from the group consisting of alkylamino, alkyl, alkenyl, alkynyl, alkyl(carboxyl), alkyl(hydroxy), alkyl(phosphonate), alkyl(sulfonate), aryl, alkylaminoalkyl, alkoxyalkyl, alkylthioalkyl, alkylthio, alicyclic, 1,1-dihaloalkyl, carbonylalkyl, aminocarbonylamino, alkylaminocarbonyl, alkylcarbonylamino, aralkyl, and alkylaryl, all optionally substituted; or] together with Y forms a cyclic group [including] selected from the group of cyclic alkyl, heterocyclic, and aryl;

[Y is selected from the group consisting of -H, alkyl, alkenyl, alkynyl, aryl, alicyclic, aralkyl, aryloxyalkyl, alkoxyalkyl, -C(O)R³, -S(O)₂R³, -C(O)-OR³, -CONHR³, -NR²₂, and -OR³, all except H are optionally substituted; or together with X forms a cyclic group including aryl, cyclic alkyl, and heterocyclic;]

R¹ is independently selected from the group consisting of -H, alkyl, aryl, [alicyclic] heteroalicyclic where the cyclic moiety contains a carbonate or thiocarbonate, -C(R²)₂-aryl, [alkylaryl] -alk-aryl, -C(R²)₂OC(O)NR²₂, -NR²-C(O)-R³, -C(R²)₂-OC(O)R³, -C(R²)₂-O-C(O)OR³, -C(R²)₂OC(O)SR³, [alkyl-S-C(O)R³] -alk-S-C(O)R³, [alkyl-S-S-alkylhydroxy] -alk-S-S-alkylhydroxy, and [alkyl-S-S-S-alkylhydroxy] -alk-S-S-S-alkylhydroxy, or together R¹ and R¹ are [-alkyl-S-S-alkyl-] -alk-S-S-alk- to form a cyclic group, wherein each "alk" is an independently selected alkylene, or together R¹ and R¹ are



wherein

V and W are independently selected from the group consisting of hydrogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, 1-alkynyl, and -R⁹; or

together V and Z are connected via a chain of 3-5 atoms, [optionally 1 heteroatom] only one of which can be a heteroatom, to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxy carboxy, or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus; or

together V and W are connected via a chain of [to form a cyclic group containing] 3 carbon atoms to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxy carboxy, alkylthiocarboxy, hydroxymethyl, [and] or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus;

Z is selected from the group consisting of -CH₂OH, -CH₂OCOR³, -CH₂OC(O)SR³, -CH₂OCO₂R³, -SR³, -S(O)R³, -CH₂N₃, -CH₂NR²₂, -CH₂Ar, -CH(Ar)OH, -CH(CH=CR²R²)OH, -CH(C≡CR²)OH, and -R²;

with the provisos that:

- a) V, Z, W are not all -H; and
- b) when Z is -R², then at least one of V and W is not -H or -R⁹;

R² is selected from the group consisting of R³ and -H;

R³ is selected from the group consisting of alkyl, aryl, alicyclic, heteroalicyclic, and aralkyl;

R⁴ is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, and lower aryl;

R⁵ is selected from the group consisting of lower alkyl, lower aryl, lower aralkyl, lower heteroalicyclic, and lower alicyclic;

R⁶ is independently selected from the group consisting of -H, and lower alkyl;

R⁷ is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, lower aryl, and -C(O)R¹⁰;

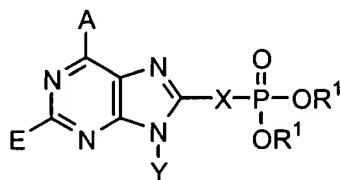
R^8 is independently selected from the group consisting of -H, lower alkyl, lower aralkyl, lower aryl, lower alicyclic, $-C(O)R^{10}$, or together [they] said R^8 groups form a bidendate [alkyl] alkylene;

R^9 is selected from the group consisting of alkyl, aralkyl, heteroalicyclic, and alicyclic;

R^{10} is selected from the group consisting of -H, lower alkyl, $-NH_2$, lower aryl, and lower perhaloalkyl;

R^{11} is selected from the group consisting of alkyl, aryl, $-OH$, $-NH_2$ and $-OR^3$; and pharmaceutically acceptable prodrugs and salts thereof.

36. A method of inhibiting FBPase at the AMP site in patients in need thereof, comprising administering to said patients an FBPase inhibitory amount of a compound of formula (1):



wherein

A is selected from the group consisting of $-NR^8_2$, $-NHSO_2R^3$, $-OR^5$, $-SR^5$, [halogen] halo, lower alkyl, $-CON(R^4)_2$, [guanidine, amidine,] guanidino, amidino, -H, and perhaloalkyl;

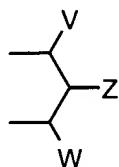
E is selected from the group consisting of -H, [halogen] halo, lower alkylthio, lower perhaloalkyl, lower alkyl, lower alkenyl, lower alkynyl, lower alkoxy, -CN, and $-NR^7_2$;

X [is selected from the group consisting of alkylamino, alkyl, alkenyl, alkynyl, alkyl(carboxyl), alkyl(hydroxy), alkyl(phosphonate), alkyl(sulfonate), aryl, alkylaminoalkyl, alkoxyalkyl, alkylthioalkyl, alkylthio, alicyclic, 1,1-dihaloalkyl, carbonylalkyl, aminocarbonylamino, alkylaminocarbonyl, alkylcarbonylamino, aralkyl, and alkylaryl, all optionally substituted; or] together with Y forms a cyclic group [including] selected from the group of cyclic alkyl, heterocyclic, and aryl;

[Y is selected from the group consisting of -H, alkyl, alkenyl, alkynyl, aryl, alicyclic, aralkyl, aryloxyalkyl, alkoxyalkyl, $-C(O)R^3$, $-S(O)_2R^3$, $-C(O)-OR^3$, $-CONHR^3$, $-NR^2_2$, and $-OR^3$,

all except H are optionally substituted; or together with X forms a cyclic group including aryl, cyclic alkyl, and heterocyclic;]

R^1 is independently selected from the group consisting of -H, alkyl, aryl, [alicyclic] heteroalicyclic where the cyclic moiety contains a carbonate or thiocarbonate, $-C(R^2)_2\text{-aryl}$, [alkylaryl] -alk-aryl, $-C(R^2)_2\text{OC(O)NR}^2_2$, $-\text{NR}^2\text{-C(O)-R}^3$, $-C(R^2)_2\text{-OC(O)R}^3$, $-C(R^2)_2\text{-O-C(O)OR}^3$, $-C(R^2)_2\text{OC(O)SR}^3$, [alkyl-S-C(O)R³] -alk-S-C(O)R³, [alkyl-S-S-alkylhydroxy] -alk-S-S-alkylhydroxy, and [alkyl-S-S-S-alkylhydroxy] -alk-S-S-S-alkylhydroxy, or together R^1 and R^1 are [-alkyl-S-S-alkyl-] -alk-S-S-alk- to form a cyclic group, wherein each "alk" is an independently selected alkylene, or together R^1 and R^1 are



wherein

V and W are independently selected from the group consisting of hydrogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, 1-alkynyl, and $-R^9$; or

together V and Z are connected via a chain of 3-5 atoms, [optionally 1 heteroatom] only one of which can be a heteroatom, to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxy carboxy, or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus; or

together V and W are connected via a chain of [to form a cyclic group containing] 3 carbon atoms to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxy carboxy, alkylthiocarboxy, hydroxymethyl, [and] or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus;

Z is selected from the group consisting of $-\text{CH}_2\text{OH}$, $-\text{CH}_2\text{OCOR}^3$, $-\text{CH}_2\text{OC(O)SR}^3$, $-\text{CH}_2\text{OCO}_2\text{R}^3$, $-\text{SR}^3$, $-\text{S(O)R}^3$, $-\text{CH}_2\text{N}_3$, $-\text{CH}_2\text{NR}^2_2$, $-\text{CH}_2\text{Ar}$, $-\text{CH(Ar)OH}$, $-\text{CH(CH=CR}^2\text{R}^2\text{)OH}$, $-\text{CH(C}\equiv\text{CR}^2\text{)OH}$, and $-R^2$;

with the provisos that:

- a) V, Z, W are not all -H; and
- b) when Z is $-R^2$, then at least one of V and W is not -H or $-R^9$;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, heteroalicyclic, and aralkyl;

R^4 is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, and lower aryl;

R^5 is selected from the group consisting of lower alkyl, lower aryl, lower aralkyl, lower heteroalicyclic, and lower alicyclic;

R^6 is independently selected from the group consisting of -H, and lower alkyl;

R^7 is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, lower aryl, and $-C(O)R^{10}$;

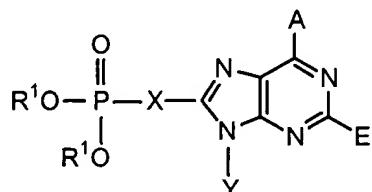
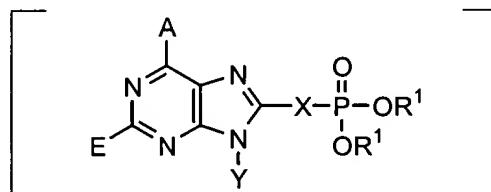
R^8 is independently selected from the group consisting of -H, lower alkyl, lower aralkyl, lower aryl, lower alicyclic, $-C(O)R^{10}$, or together [they] said R^8 groups form a bidendate [alkyl] alkylene;

R^9 is selected from the group consisting of alkyl, aralkyl, heteroalicyclic, and alicyclic;

R^{10} is selected from the group consisting of -H, lower alkyl, $-NH_2$, lower aryl, and lower perhaloalkyl;

R^{11} is selected from the group consisting of alkyl, aryl, $-OH$, $-NH_2$ and $-OR^3$; and pharmaceutically acceptable prodrugs and salts thereof.

37. (Amended) A method of inhibiting gluconeogenesis in animal in need thereof, comprising administering to said animal an effective amount of a compound of formula (1):



wherein

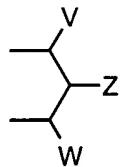
A is selected from the group consisting of -NR⁸₂, -NHSO₂R³, -OR⁵, -SR⁵, [halogen] halo, lower alkyl, -CON(R⁴)₂, [guanidine, amidine,] guanidino, amidino, -H, and perhaloalkyl;

E is selected from the group consisting of -H, [halogen] halo, lower alkylthio, lower perhaloalkyl, lower alkyl, lower alkenyl, lower alkynyl, lower alkoxy, -CN, and -NR⁷₂;

X [is selected from the group consisting of alkylamino, alkyl, alkenyl, alkynyl, alkyl(carboxyl), alkyl(hydroxy), alkyl(phosphonate), alkyl(sulfonate), aryl, alkylaminoalkyl, alkoxyalkyl, alkylthioalkyl, alkylthio, alicyclic, 1,1-dihaloalkyl, carbonylalkyl, aminocarbonylamino, alkylaminocarbonyl, alkylcarbonylamino, aralkyl, and alkylaryl, all optionally substituted; or] together with Y forms a cyclic group [including selected from the group of cyclic alkyl, heterocyclic, and aryl];

[Y is selected from the group consisting of -H, alkyl, alkenyl, alkynyl, aryl, alicyclic, aralkyl, aryloxyalkyl, alkoxyalkyl, -C(O)R³, -S(O)₂R³, -C(O)-OR³, -CONHR³, -NR²₂, and -OR³, all except H are optionally substituted; or together with X forms a cyclic group including aryl, cyclic alkyl, and heterocyclic;]

R¹ is independently selected from the group consisting of -H, alkyl, aryl, [alicyclic] heteroalicyclic where the cyclic moiety contains a carbonate or thiocarbonate, -C(R²)₂-aryl, [alkylaryl] -alk-aryl, -C(R²)₂OC(O)NR²₂, -NR²-C(O)-R³, -C(R²)₂-OC(O)R³, -C(R²)₂-O-C(O)OR³, -C(R²)₂OC(O)SR³, [alkyl-S-C(O)R³] -alk-S-C(O)R³, [alkyl-S-S-alkylhydroxy] -alk-S-S-alkylhydroxy, and [alkyl-S-S-S-alkylhydroxy] -alk-S-S-S-alkylhydroxy, or together R¹ and R¹ are [-alkyl-S-S-alkyl-] -alk-S-S-alk- to form a cyclic group, wherein each "alk" is an independently selected alkylene, or together R¹ and R¹ are



wherein

V and W are independently selected from the group consisting of hydrogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, 1-alkynyl, and -R⁹; or

together V and Z are connected via a chain of 3-5 atoms, [optionally 1 heteroatom] only one of which can be a heteroatom, to form part of a cyclic group substituted with hydroxy,

acyloxy, alkoxy carboxy, or aryloxy carboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus; or

together V and W are connected via a chain of [to form a cyclic group containing] 3 carbon atoms to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxy carboxy, alkylthiocarboxy, hydroxymethyl, [and] or aryloxy carboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus;

Z is selected from the group consisting of -CH₂OH, -CH₂OCOR³, -CH₂OC(O)SR³, -CH₂OCO₂R³, -SR³, -S(O)R³, -CH₂N₃, -CH₂NR²₂, -CH₂Ar, -CH(Ar)OH, -CH(CH=CR²R²)OH, -CH(C≡CR²)OH, and -R²;

with the provisos that:

- a) V, Z, W are not all -H; and
- b) when Z is -R², then at least one of V and W is not -H or -R⁹;

R² is selected from the group consisting of R³ and -H;

R³ is selected from the group consisting of alkyl, aryl, alicyclic, heteroalicyclic, and aralkyl;

R⁴ is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, and lower aryl;

R⁵ is selected from the group consisting of lower alkyl, lower aryl, lower aralkyl, lower heteroalicyclic, and lower alicyclic;

R⁶ is independently selected from the group consisting of -H, and lower alkyl;

R⁷ is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, lower aryl, and -C(O)R¹⁰;

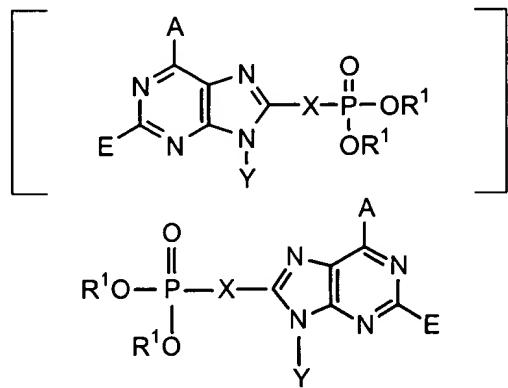
R⁸ is independently selected from the group consisting of -H, lower alkyl, lower aralkyl, lower aryl, lower alicyclic, -C(O)R¹⁰, or together [they] said R⁸ groups form a bidendate [alkyl] alkylene;

R⁹ is selected from the group consisting of alkyl, aralkyl, heteroalicyclic, and alicyclic;

R¹⁰ is selected from the group consisting of -H, lower alkyl, -NH₂, lower aryl, and lower perhaloalkyl;

R¹¹ is selected from the group consisting of alkyl, aryl, -OH, -NH₂ and -OR³; and pharmaceutically acceptable prodrugs and salts thereof.

39. (Amended) A method of treating an animal for a disease derived from abnormally elevated insulin levels, comprising administering to said animal a therapeutically effective amount of a fructose-1,6-bisphosphatase inhibitor wherein said inhibitor is a compound of formula (1):



wherein

A is selected from the group consisting of -NR⁸, -NHSO₂R³, -OR⁵, -SR⁵, [halogen] halo, lower alkyl, -CON(R⁴)₂, [guanidine, amidine,] guanidino, amidino, -H, and perhaloalkyl;

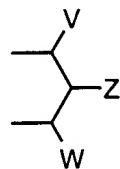
E is selected from the group consisting of -H, [halogen] halo, lower alkylthio, lower perhaloalkyl, lower alkyl, lower alkenyl, lower alkynyl, lower alkoxy, -CN, and -NR⁷₂;

X is selected from the group consisting of alkylamino, alkyl, alkenyl, alkynyl, alkyl(carboxyl), alkyl(hydroxy), alkyl(phosphonate), alkyl(sulfonate), aryl, alkylaminoalkyl, alkoxyalkyl, alkylthioalkyl, alkylthio, alicyclic, 1,1-dihaloalkyl, carbonylalkyl, aminocarbonylamino, alkylaminocarbonyl, alkylcarbonylamino, aralkyl, and alkylaryl, all optionally substituted; or] together with Y forms a cyclic group [including selected from the group of cyclic alkyl, heterocyclic, and aryl;

[Y is selected from the group consisting of -H, alkyl, alkenyl, alkynyl, aryl, alicyclic, aralkyl, aryloxyalkyl, alkoxyalkyl, -C(O)R³, -S(O)₂R³, -C(O)-OR³, -CONHR³, -NR²₂, and -OR³, all except H are optionally substituted; or together with X forms a cyclic group including aryl, cyclic alkyl, and heterocyclic;]

R¹ is independently selected from the group consisting of -H, alkyl, aryl, [alicyclic] heteroalicyclic where the cyclic moiety contains a carbonate or thiocarbonate, -C(R²)₂-aryl, [alkylaryl] -alk-aryl, -C(R²)₂OC(O)NR²₂, -NR²-C(O)-R³, -C(R²)₂-OC(O)R³, -C(R²)₂-O-C(O)OR³, -C(R²)₂OC(O)SR³, [alkyl-S-C(O)R³] -alk-S-C(O)R³, [alkyl-S-S-alkylhydroxy] -alk-S-S-alkylhydroxy, and [alkyl-S-S-S-alkylhydroxy] -alk-S-S-S-alkylhydroxy, or together R¹ and

R^1 are [-alkyl-S-S-alkyl-] -alk-S-S-alk- to form a cyclic group, wherein each "alk" is an independently selected alkylene, or together R^1 and R^1 are



wherein

V and W are independently selected from the group consisting of hydrogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, 1-alkynyl, and $-R^9$; or

together V and Z are connected via a chain of 3-5 atoms, [optionally 1 heteroatom] only one of which can be a heteroatom, to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxy carboxy, or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus; or

together V and W are connected via a chain of [to form a cyclic group containing] 3 carbon atoms to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxy carboxy, alkylthiocarboxy, hydroxymethyl, [and] or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus;

Z is selected from the group consisting of $-CH_2OH$, $-CH_2OCOR^3$, $-CH_2OC(O)SR^3$, $-CH_2OCO_2R^3$, $-SR^3$, $-S(O)R^3$, $-CH_2N_3$, $-CH_2NR^2_2$, $-CH_2Ar$, $-CH(Ar)OH$, $-CH(CH=CR^2R^2)OH$, $-CH(C\equiv CR^2)OH$, and $-R^2$;

with the provisos that:

- a) V, Z, W are not all -H; and
- b) when Z is $-R^2$, then at least one of V and W is not -H or $-R^9$;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, heteroalicyclic, and aralkyl;

R^4 is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, and lower aryl;

R^5 is selected from the group consisting of lower alkyl, lower aryl, lower aralkyl, lower heteroalicyclic, and lower alicyclic;

R^6 is independently selected from the group consisting of -H, and lower alkyl;

R^7 is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, lower aryl, and $-C(O)R^{10}$;

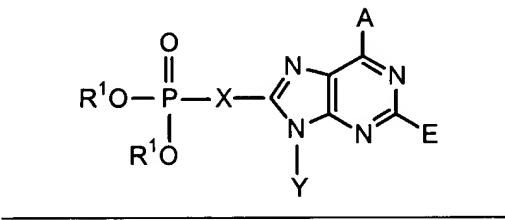
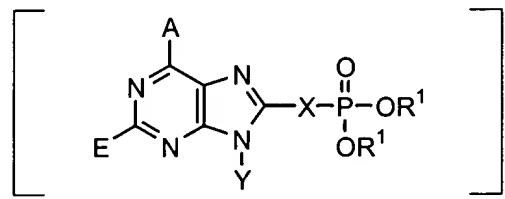
R^8 is independently selected from the group consisting of -H, lower alkyl, lower aralkyl, lower aryl, lower alicyclic, $-C(O)R^{10}$, or together [they] said R^8 groups form a bidendate [alkyl] alkylene;

R^9 is selected from the group consisting of alkyl, aralkyl, heteroalicyclic, and alicyclic;

R^{10} is selected from the group consisting of -H, lower alkyl, $-NH_2$, lower aryl, and lower perhaloalkyl;

R^{11} is selected from the group consisting of alkyl, aryl, $-OH$, $-NH_2$ and $-OR^3$; and pharmaceutically acceptable prodrugs and salts thereof.

42. (Amended) A method of treating an animal with excess glycogen storage disease, comprising administering to said animal in need thereof a therapeutically effective amount of a fructose-1,6-bisphosphatase inhibitor, wherein said inhibitor is a compound of formula (1):



wherein

A is selected from the group consisting of $-NR^8_2$, $-NHSO_2R^3$, $-OR^5$, $-SR^5$, [halogen] halo, lower alkyl, $-CON(R^4)_2$, [guanidine, amidine,] guanidino, amidino, -H, and perhaloalkyl;

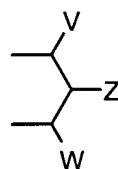
E is selected from the group consisting of -H, [halogen] halo, lower alkylthio, lower perhaloalkyl, lower alkyl, lower alkenyl, lower alkynyl, lower alkoxy, -CN, and $-NR^7_2$;

X [is selected from the group consisting of alkylamino, alkyl, alkenyl, alkynyl, alkyl(carboxyl), alkyl(hydroxy), alkyl(phosphonate), alkyl(sulfonate), aryl, alkylaminoalkyl, alkoxyalkyl, alkylthioalkyl, alkylthio, alicyclic, 1,1-dihaloalkyl, carbonylalkyl,

aminocarbonylamino, alkylaminocarbonyl, alkylcarbonylamino, aralkyl, and alkylaryl, all optionally substituted; or] together with Y forms a cyclic group [including] selected from the group of cyclic alkyl, heterocyclic, and aryl;

[Y is selected from the group consisting of -H, alkyl, alkenyl, alkynyl, aryl, alicyclic, aralkyl, aryloxyalkyl, alkoxyalkyl, -C(O)R³, -S(O)₂R³, -C(O)-OR³, -CONHR³, -NR²₂, and -OR³, all except H are optionally substituted; or together with X forms a cyclic group including aryl, cyclic alkyl, and heterocyclic;]

R¹ is independently selected from the group consisting of -H, alkyl, aryl, [alicyclic] heteroalicyclic where the cyclic moiety contains a carbonate or thiocarbonate, -C(R²)₂-aryl, [alkylaryl] -alk-aryl, -C(R²)₂OC(O)NR², -NR²-C(O)-R³, -C(R²)₂-OC(O)R³, -C(R²)₂-O-C(O)OR³, -C(R²)₂OC(O)SR³, [alkyl-S-C(O)R³] -alk-S-C(O)R³, [alkyl-S-S-alkylhydroxy] -alk-S-S-alkylhydroxy, and [alkyl-S-S-S-alkylhydroxy] -alk-S-S-S-alkylhydroxy, or together R¹ and R¹ are [-alkyl-S-S-alkyl-] -alk-S-S-alk- to form a cyclic group, wherein each "alk" is independently selected alkylene, or together R¹ and R¹ are



wherein

V and W are independently selected from the group consisting of hydrogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, 1-alkynyl, and -R⁹; or

together V and Z are connected via a chain of 3-5 atoms, [optionally 1 heteroatom] only one of which can be a heteroatom, to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxy, alkoxycarboxy, or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus; or

together V and W are connected via a chain of [to form a cyclic group containing] 3 carbon atoms to form part of a cyclic group substituted with hydroxy, acyloxy, alkoxy, alkoxycarboxy, alkylthiocarboxy, hydroxymethyl, [and] or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus;

Z is selected from the group consisting of -CH₂OH, -CH₂OCOR³, -CH₂OC(O)SR³, -CH₂OCO₂R³, -SR³, -S(O)R³, -CH₂N₃, -CH₂NR²₂, -CH₂Ar, -CH(Ar)OH, -CH(CH=CR²R²)OH, -CH(C≡CR²)OH, and -R²;

with the provisos that:

a) V, Z, W are not all -H; and

b) when Z is -R², then at least one of V and W is not -H or -R⁹;

R² is selected from the group consisting of R³ and -H;

R³ is selected from the group consisting of alkyl, aryl, alicyclic, heteroalicyclic, and aralkyl;

R⁴ is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, and lower aryl;

R⁵ is selected from the group consisting of lower alkyl, lower aryl, lower aralkyl, lower heteroalicyclic, and lower alicyclic;

R⁶ is independently selected from the group consisting of -H, and lower alkyl;

R⁷ is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower heteroalicyclic, lower aralkyl, lower aryl, and -C(O)R¹⁰;

R⁸ is independently selected from the group consisting of -H, lower alkyl, lower aralkyl, lower aryl, lower alicyclic, -C(O)R¹⁰, or together [they] said R⁸ groups form a bidendate [alkyl] alkylene;

R⁹ is selected from the group consisting of alkyl, aralkyl, heteroalicyclic, and alicyclic;

R¹⁰ is selected from the group consisting of -H, lower alkyl, -NH₂, lower aryl, and lower perhaloalkyl;

R¹¹ is selected from the group consisting of alkyl, aryl, -OH, -NH₂ and -OR³; and pharmaceutically acceptable prodrugs and salts thereof.